

In the Specification

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Please amend the first full paragraph on page 29 as follows:

B
The membrane-permeant antagonists 7-deaza-8-Br-cADPR and xestospongine C are powerful tools, but to achieve a sufficiently high intracellular effective concentration, a substantial preincubation period must be employed. To find out whether either Ins(1,4,5) P₃ or cADPR or both play an essential role also at a later time point after TCR/CD3 stimulation, we stimulated the cells by OKT3, and, after development of Ca²⁺ signalling, microinjected a specific antagonist, e.g. inositol 1,4,6-triphosphorothioate (Ins(1,4,6)P₃S₃), or 8-methoxy-cADPR, or a combination of both (Figure 3). Following the development of Ca²⁺ signalling stimulation by OKT3, microinjection of 8-methoxy-cADPR, a novel cADPR antagonist of similar potency as 8-NH₂-cADPR, significantly decreased the magnitude of further Ca²⁺ signals (Figure 3a, b, e), whereas microinjection of Ins(1,4,6) P₃ S₃ did not have a significant effect (Figure 3a, c, e). Combined microinjection of 8-methoxy-cADPR and Ins(1,4,6)P₃ S₃ resulted in a somewhat more pronounced inhibition as compared to 8-methoxy-cADPR alone (Figure 3e). These data confirm the concept of both an initial Ca²⁺ signalling phase for which Ins(1,4,5)P₃ is essential, and a sustained phase driven mainly by cADPR.
